

EFED BIOTECHNOLOGY REVIEW

Pesticide Name 1,4-Dimethylnaphthalene

Reviewed By:

David Bays, PhD
Microbiologist
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David Bays
8/31/94

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8/31/94

100.0.0 Submission Purpose and Label Information

100.1.0 Submission Purpose and Pesticide Use

D-I-1-4, Inc. has requested a Section 3 Registration for 1,4-dimethylnaphthalene. This product is used as an aerosol to control sprouting of potatoes during the storage phase.

100.2.0 Formulation Information

1.4SIGHT

Aerosol Grade-Potato Sprout Inhibitor

	By Weight
ACTIVE INGREDIENT: 1,4-Dimethylnaphthalene*	94.7%
Inert Ingredients	3.6%
TOTAL	100.00%

*Contains 7.9 pounds active ingredient per gallon.

100.3.0 Application Methods, Directions, Rates

See attached label.

100.4.0 Target Organisms

Not Applicable, because this product acts as a sprout inhibitor in potatoes.

100.5.0 Precautionary Labeling

The label contains the following precautions:

KEEP OUT OF REACH OF CHILDREN

CAUTION

HAZARDS TO HUMANS (AND DOMESTIC ANIMALS): (adequate)

(Pesticide and container disposal directions are adequate)

Environmental Hazards

Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water by disposal of equipment wash waters.

101.0.0 Hazard Assessment

101.1.0 Discussion

The studies supplied with this submission will be considered core and fulfill EPA Guideline requirements. The results indicate that Naphthalene is highly toxic to freshwater invertebrates and fish, and practically nontoxic to birds (on an acute basis). Therefore, Naphthalene should not pose an adverse risk to birds, but may pose an adverse risk to aquatic organisms.

101.2.0 Likelihood at Adverse Effects to Nontarget Organisms

Avian Studies

Submitted study entitled "An Acute LD₅₀ Study, Species: Northern Bobwhite Quail (*Colinus virginianus*)" (MRID #430825-19) shows that the acute oral LD₅₀ value for northern bobwhite exposed to Naphthalene was greater than 2,000 mg a.i./kg (practically nontoxic). The no observed effect dosage was 2,000 mg a.i./kg.

The results of this study indicates that Naphthalene should not cause any adverse effects to avian wildlife.

Fish Studies

Submitted study entitled "1,4-dimethylnaphthalene - Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*)" (MRID #430825-20) demonstrated the 96 hour LC₅₀ was 0.67

mg a.i./L. The 96 hour NOEL was 0.19 mg a.i./L.

The above data indicate that Naphthalene is highly toxic to freshwater fish species and could potentially cause adverse effects to nontarget freshwater fish.

Mammalian Wildlife

The data submitted to the toxicology branch indicate that there is no significant toxicity to rodents from acute oral testing at the maximum hazard dose. In light of the above results, risk to mammalian wildlife is expected to be minimal to nonexistent.

Aquatic Invertebrate Studies

In a study entitled "1,4-Dimethylnaphthalene-Acute toxicity to daphnids (Daphnia magna) under flow-through conditions" (MRID #430825-21) the 48-hour EC₅₀ was determined to be 0.54 mg a.i./L. The NOEL was considered to be 0.10 mg a.i./L.

The above data indicates that Naphthalene is highly toxic to aquatic invertebrate species and could potentially cause adverse effects to this species.

Nontarget Plant Studies

None submitted. Plant testing of biochemical pest control agents is conditionally required when there is published evidence that the compound is toxic to plants. To the best of our knowledge, this compound is not known to be toxic to plants.

Honey Bee Studies

None submitted. These studies are conditionally required and will not be required for this product.

Endangered Species Considerations

No risk to endangered species is expected from the use of this product.

101.4.0 Adequacy of Toxicity Data

(See the Generic Data Table)

The registrant has addressed the data requirements outlined in the Pesticide Assessment Guidelines, Subdivision M.

Generic Data Requirements For Naphthalene

Data Requirement	Test ¹ Substance	Use ² Patterns	Does EPA Have Data?	Bibliographic Citation	Must Additional Data Be Submitted?
<u>§158.740 Microbial Pesticide Nontarget Organism - Tier 1</u>					
<u>Avian Testing</u>					
154-6 Avian Acute Oral					
- upland gamebird	TGAI	A,I	Yes	430825-19	No
154-7 Avian Dietary					
- upland gamebird	TGAI	A,I	No	---	No ⁴
<u>Aquatic Organism Testing</u>					
154-8 Freshwater Fish LC ₅₀					
- rainbow trout	TGAI	A,I	Yes	430825-20	No
154-9 Freshwater Invertebrate					
- <u>Daphnia magna</u>	TGAI	A,I	Yes	430825-21	No
<u>Additional Testing</u>					
154-10 Nontarget plant studies					
- terrestrial	TGAI	A,I	No	---	No ⁴
- aquatic	TGAI	A,I	No	---	No ⁴
154-11 Nontarget insect testing					
- honey bee	TGAI	A,I	No	---	No ⁵

¹TGAI = Technical Grade of the Active Ingredient; TEP = Typical End-Use Product.

²The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Nonfood; C = Aquatic, Food Crop; D = Aquatic, Nonfood; E = Greenhouse, Food Crop; F = Greenhouse, Nonfood; G = Forestry; H = Domestic, Outdoor; I = Indoor.

³This data requirement is not required if the pesticide is highly volatile. In this case, Naphthalene is applied to stored potatoes as a highly volatile aerosol.

⁴Not required for this use pattern.

⁵Conditionally required for biochemicals. Not required in this case.

101.5.0 Adequacy of Labeling

The precautionary labeling (see sec. 100.5.0) is adequate except that the following statement will need to be added as the first sentence in the Environmental Hazards portion of the label: This product is highly toxic to freshwater fish and aquatic invertebrates.

102.0.0 Classification N/A

103.0.0 Conclusions

EEB has reviewed the proposed Section 3 Registration of Naphthalene by D-I-1-4, Inc. for the control of sprouting of potatoes during storage.

The studies supplied with this submission indicate that Naphthalene is practically nontoxic to avian species using an acute route of exposure, and did not demonstrate any toxicity to rodents in studies submitted to the Healthy Effects Division of OPP. However, the compound is highly toxic to freshwater fish and aquatic invertebrates. Even though this product is highly toxic to these aquatic species, it should not pose a risk to these organisms based on a lack of exposure due to its use pattern. Naphthalene is applied as an aerosol to potato tubers in storage buildings.

However, to better document this risk to aquatic organisms, the registrant should add the following statement to the Environmental Hazards Section of its label: This product is highly toxic to freshwater fish and aquatic invertebrates.

Therefore, Naphthalene should not cause any adverse effects to nontarget wildlife as long as exposure to aquatic organisms is minimized through the restricted use pattern. If the use pattern changes, then a second risk assessment will need to be completed.

DATA EVALUATION REPORT

1. Chemical: 1,4-Dimethylnaphthalene
2. Test Material: Technical
3. Study/Action Type: An Acute LD₅₀ Study, Species: Northern Bobwhite Quail (Colinus virginianus) (154B-6)
4. Study Identification: Acute Oral LD₅₀ with Bobwhite Quail (Colinus virginianus), By Md. Sayed Ahmed, PhD. Prepared By Genesis Laboratories, Inc. October 1993. Project No. 93004. Submitted By D-I-1-4, Inc., Boise, Idaho. EPA Acc. No. 430825-19.

5. Reviewed By: David C. Bays, PhD.
Biotech Review Team
EFED

Signature: *D.C. Bays*

Date: 8/31/94

Robert Pilsucki
Biotech Review Team
EFED

Signature: *Robert Pilsucki*

Date: 8/31/94

6. Conclusions:

The study is scientifically sound and demonstrated an LD₅₀ > 2,000 mg a.i./kg and the no observed effect level of 2,000 mg a.i./kg. This indicates that Naphthalene is practically non-toxic to birds on an acute basis.

7. Recommendations: N/A

8. Background:

This study was submitted to support the request for a Section 3 Registration of the biochemical pesticide 1,4-dimethylnaphthalene.

9. Materials and Methods:

- A. Test Organisms: Healthy northern bobwhite quail, 17 weeks of age and phenotypically indistinguishable from wild birds, were obtained from Barrett's Quail Farm. The quail were distributed into one test group and one control group of 10 birds each, 5 males and 5 females, for a limit dose test. The test birds were acclimated to the facilities for 15 days prior to the beginning of the study. Tap water and feed, Purina Game Bird Maintenance Chow, were provided ad libitum during the acclimation and testing periods.
- B. Dosage Form: The test substance, a colorless liquid (reported purity of 96.4%), was administered as an oral dose by capsule. The control birds received blank capsules.

The test birds were fasted for at least 17 hours before dosing. The test substance concentration was adjusted to provide a constant volume to body weight dosage for all test birds (mg/test substance per kg/body weight), but was not adjusted for the purity of the test substance. The nominal dosage used in this limit dose study was 2000 mg a.i./kg of body weight.

- C. Referenced Protocol: The dosages used in the study were established using known toxicity data. The birds were given a single oral dose of the test substance by capsule at the beginning of the study. The control consisted of birds given blank capsules.

All birds were tested in pens (90x60x45 cm) assigned by random draw and housed indoors. Average ambient room temperature for the study varied from 74F to 65F with an average relative humidity between 66% and 52%. The photoperiod (monitored by a time clock) was 10 hours of light per day during acclimation and throughout the study. Housing and husbandry practices were based upon the "Guide for the Care and Use of Laboratory Animals", NIH Publication No. 85-23, 1985.

All birds were observed daily during acclimation and any exhibiting abnormal behavior or physical injury were not used. After test initiation and continuing until termination, all birds were observed at least twice daily with all mortality, signs of toxicity or abnormal behavior being recorded. Body weights of the test birds were recorded individually prior to dosing, on Day 3, Day 7, and Day 14. Average estimated feed consumption was measured daily.

- D. Statistical Analysis: The test data in this study was not statistically analyzed because of a lack of mortalities.

12. Reported Results:

<u>Dosage</u>	<u>mg/kg</u>	<u>Number Dead/Number Exposed</u> <u>(At 14 Days After Dosing)</u>
Control		0/12
Treatment	2000	0/12
LD ₅₀ < 2,000 mg a.i./kg		

No mortalities occurred with any of the control or treated birds.

13. Study Author's Conclusions/Quality Assurance Measures:

$LD_{50} < 2,000$ mg a.i./kg

"This study contained herein, 93004, was conducted in accordance with the requirements of Title 40, Code of Federal Regulations, Part 160, Good Laboratory Practice Standards. The raw data have been reviewed by the study Director who certifies that the information contained in this report is consistent with the data within the context of the study design and evaluation criteria." Signed by study director, Md. Sayed Ahmed, PhD.

14. Reviewer's Discussion and Interpretation of the Study:

- A. Test Procedures: The procedures used followed those recommended by EPA in Section 154-6 of the EPA Registration Guidelines (Pesticide Assessment Guidelines, FIFRA Subdivision M, Microbial and Biochemical Pest Control Agents).
- B. Statistical Analysis: No Statistical analysis was performed due to a lack of mortalities.
- C. Discussion/Results: An $LD_{50} < 2,000$ mg a.i./kg indicates that Naphthalene is practically non-toxic to birds on an acute basis.
- D. Adequacy of the Study:
 - 1. Validation Category: Core
 - 2. Rationale: The study meets guideline requirements

15. Completion of the One-liner:

DATA EVALUATION REPORT

1. Chemical: 1,4-Dimethlynaphthalene
2. Test Material: Technical.
3. Study/Action Type: Freshwater Fish LC₅₀ (154-8)
4. Study Identification: 1,4-Dimethlynaphthalene - Acute Toxicity to Rainbow Trout (Oncorhynchus mykiss) Under Flow-Through Conditions. By Michael J. Bettencourt, Study Director. Prepared By Springborn Laboratories, Inc., October 8, 1993. Project ID. #13117.0693.6101.108. Submitted By D-I-1-4, Inc., Boise, Idaho, EPA Acc. No. 430825-20.

5. Reviewed By: David C. Bays, PhD.
Biotech Review Team
EFED

Signature: *David C. Bays*

Date: 8/31/94

Bob Pilsucki, PhD.
Biotech Review Team
EFED

Signature: *Bob Pilsucki*

Date: 8/31/94

6. Conclusions:

The study is scientifically sound and demonstrated an LC₅₀ = 0.67 mg a.i./L. This indicates that Naphthalene is highly toxic to freshwater fish. The no-effect concentration at 96 hours was found to be 0.19 mg a.i./L. The 95% confidence limits were 0.57 and 0.80 mg a.i./L. The study fulfills EPA Guideline requirements for an acute toxicity test for freshwater fish.

7. Recommendations: N/A

8. Background:

This study was submitted for a Section 3 registration of the biochemical pesticide Naphthalene.

10. Materials and Methods:

- A. Test Organisms: The rainbow trout used in this study were obtained from Mt. Lassen Trout Farm in Red Bluff, California. The fish (mean weight 1.5 g [0.8 to 2.8] and a mean length of 50 [42 to 63] mm) were reared and maintained at Springborn Labs in water with a total hardness that ranged from 26 to 28 mg/l - as CaCO₃. The fish were fed salmon a dry commercial pelleted food mash, *ad libitum*, during holding, but were not fed 48 hours before test initiation or during the test.

B. Dosage Form: The test material, a clear liquid, (96.4% active ingredient) was mixed with acetone for a concentration of 5.0 mg a.i./ml. The nominal concentration regime was 0.32, 0.54, 0.90, 1.5, and 2.5 mg a.i./L. The regime was determined using preliminary static tests. The mean measured test concentrations from samples collected at 0 and 96 hours were 0.19, 0.22, 0.41, 0.75 and 1.2 mg a.i./L. The low recovery level of test material was most likely due to the limited water solubility of Naphthalene.

C. Referenced Protocol: A proportional diluter was used to provide the proper concentration of test substance to each of the test chambers (6.6 volume changes every 24 hours). The study was initiated after the test solutions had been flowing through the test chambers (glass 39X20X25 cm aquaria filled with 15 L of test solution) for several days. At this time, 10 rainbow trout were impartially distributed to each chamber, which was positioned in a temperature-controlled water bath (12 ± 1 C). The treatments included 2 replications (each containing 10 trout) of the 5 concentrations of the test material, and a dilution water control.

The water quality parameters of temperature, dissolved oxygen and Ph were measured at 0-, 48- and 96- hours and were determined to be within acceptable limits (Temp. = 11-12C; pH = 7.1-7.7; Dissolved oxygen = 8.4-9.8 mg/L). Observations for mortality and sub-lethal responses were made once every 24 hours during the 96 hour test period.

D. Statistical Analysis: The LC_{50} values and 95% confidence limits were calculated using the computer program of C.E. Stephan, which uses probit analysis, the moving average-angle method, or binomial probability method with nonlinear interpolation.

12. Reported Results:

<u>Dosage (mg/l)</u>		<u>Number Dead/Number Exposed</u> <u>(At 96 hours After Dosing)</u>
Negative Control	A	0/10
	B	0/10
Solvent Control	A	0/10
	B	0/10
0.19	A	0/10
	B	0/10
0.22	A	1/10
	B	0/10

0.41	A	0/10
	B	1/10
0.75	A	5/10
	B	4/10
1.2	A	10/10
	B	10/10

$LC_{50} = 0.67 \text{ mg a.i./L}$

The 95% confidence limits were 0.57 and 0.80 mg a.i./L and the no effects concentration was 0.19 mg a.i./L.

13. Study Author's Conclusions/Quality Assurance Measures:

$LC_{50} = 0.67 \text{ mg a.i./L}$

"The data and report presented for 1,4-Dimethylnaphthalene - Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*) Under Flow-Through Conditions were produced and compiled in accordance with all pertinent EPA Good Laboratory Practice regulations (40 CFR, Part 160) with only minor exceptions which were not significant enough to affect the integrity of the study or the interpretation of the test results."

Signed by study director: Michael J. Bettencourt

14. Reviewer's Discussion and Interpretation of the Study:

- A. Test Procedures: The procedures used followed those recommended by EPA in Section 154-8 of the EPA Registration Guidelines (Pesticide Assessment Guidelines, FIFRA Subdivision M, Microbial and Biochemical Pest Control Agents).
- B. Statistical Analysis: Binomial probability with nonlinear interpolation using the computer program of C. E. Stephan.
- C. Discussion/Results: An $LC_{50} = 0.67 \text{ mg a.i./L}$ indicates that Naphthalene is highly toxic, on an acute basis, to rainbow trout.
- D. Adequacy of the Study:
 - 1. Validation Category: Core
 - 2. Rationale: Meets EPA Guideline requirements

15. Completion of the One-Liner:

DATA EVALUATION REPORT

1. Chemical: Naphthalene
2. Test Material: Technical
3. Study/Action Type: Freshwater Invertebrate Acute EC_{50} (154-9)
4. Study Identification: 1,4-Dimethylnaphthalene-Acute Toxicity to daphnids (*Daphnia magna*) under flow-through conditions. By Arthur E. Putt, Study Director. Prepared By Springborn Laboratories, Inc., October 8, 1993 Study ID.#: 13117.0693.6102.115. Submitted By Springborn Laboratories, Wareham, Massachusetts, EPA Acc. No. 430825-21.

5. Reviewed By: David C. Bays, PhD
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Signature: *David C. Bays*

Date: 8/31/94

Signature: *Robert Pilsucki*

Date: 8/31/94

6. Conclusions:

The study is scientifically sound and demonstrated an EC_{50} = 0.54 mg/L. This indicates that Naphthalene is highly toxic to freshwater invertebrates. The no-effect concentration at 48 hours was found to be 0.10 mg/L. The study fulfills EPA Guideline requirements for an acute toxicity test for freshwater invertebrates.

7. Recommendations: N/A

8. Background:

This study was submitted to support the request for the registration of the biochemical pesticide 1,4-dimethylnaphthalene.

10. Materials and Methods:

- A. Test Organisms: Test specimens of *Daphnia magna* were obtained from in-house cultures maintained by Springborn Laboratories. During a holding period, the daphnids were fed a mixture of trout food suspension and a unicellular green algae (*Ankistrodesmus falcatus*) once daily.
- B. Dosage Form: The test material, a clear liquid, was characterized as 96.4% active ingredient and having negligible solubility in water.
- C. Referenced Protocol: The test system employed a diluter

which was calibrated to inject a stock solution into a mixing chamber which continuously stirred the solution. A mechanical injector delivered the proper amount of stock solution to each 1.6 L glass battery jar that corresponded to each test concentration. Ten daphnids/beaker (<24 hours old) were used and were added to each beaker within 30 minutes of test solution preparation. Preliminary experiments were conducted using the following exposure concentrations: 0.10, 0.50, 1.0, 5.0 mg a.i./L; 0.16, 0.26, 0.43, 0.72 and 1.2 mg a.i./L; and 0.65, 1.1, 1.8, 3.0, 5.0 mg a.i./L. Based on these results, the mean measured concentrations of 0.21, 0.33, 0.56, 0.94 and 2.2 mg a.i./L were used in this study.

The water quality parameters of temperature, dissolved oxygen and pH were measured at 0- and 48- hours and were determined to be within acceptable limits (Temp. = $20 \pm 2^\circ\text{C}$; pH = 7.9-8.3; Dissolved oxygen = 8.3-8.8 mg/L). Observations for mortality and sub-lethal responses were made at 0, 24, and 48 hours.

- D. Statistical Analysis: The EC_{50} values and 95% confidence limits were calculated using the computer program of C.E. Stephan, which uses probit analysis, the moving average-angle method, or binomial probability method with nonlinear interpolation.

12. Reported Results:

<u>Dosage(mg/l)</u>	<u>Replicate</u>	<u>Number Dead/Number Exposed</u> <u>(At 48 hours After Dosing)</u>
Control	A	0/10
	B	0/10
Solvent Control	A	0/10
	B	0/10
0.056	A	0/10
	B	0/10
0.10	A	0/10
	B	0/10
0.18	A	0/10
	B	10/10
0.31	A	0/10
	B	10/10
0.48	A	10/10
	B	10/10

$EC_{50} = 0.54$ mg a.i./L (95% confidence levels=0.33 to 0.94 mg a.i./L-calculated by binomial probability)

13. Study Author's Conclusions/Quality Assurance Measures:

$EC_{50} = 0.54$ mg a.i./L

"The data and report prepared for 1,4-Dimethylnaphthalene-Acute Toxicity To Daphnids (*Daphnia magna*) Under Flow-Through Conditions were produced and compiled in accordance with all pertinent U.S. EPA Good Laboratory Practice Standards; Pesticide Programs (40 CFR 160) with only minor exceptions which did not affect the integrity of the study or the interpretation of the test results. "

Signed by study director: Arthur E. Putt, Study Director

14. Reviewer's Discussion and Interpretation of the Study:

A. Test Procedures: The procedures used followed those recommended by EPA in Section 154-9 of the EPA Registration Guidelines (Pesticide Assessment Guidelines, FIFRA Subdivision M, Microbial and Biochemical Pest Control Agents).

B. Statistical Analysis: Computer program of C. E. Stephan.

C. Discussion/Results: An $EC_{50} = 0.54$ mg a.i./L indicates that Naphthalene is highly toxic, on an acute basis, to daphnids.

D. Adequacy of the Study:

1. Validation Category: Core

2. Rationale: Meets EPA Guideline requirements

15. Completion of the One-Liner: